

William E. Rich, et al.
Application No.: 09/560,715
Page 2

PATENT

B1
A2 3 and a hydrogel material on the surface, wherein the hydrogel material is crosslinked and
4 comprises binding functionalities for binding with an analyte detectable by the mass
5 spectrometer.

A2 1 B1 3. (Once amended) The probe of claim 1 wherein the substrate
2 comprises an electrically conducting material.

A3 1 8. (Once amended) The probe of claim 1 wherein the hydrogel
2 material is in situ polymerized on the silicon oxide coating by depositing a solution
3 comprising monomers onto the glass coating, wherein the monomers are pre-
4 functionalized to provide binding functionalities.

B1
1 9. (Once amended) The probe of claim 1 wherein the thickness of the
2 coating and the hydrogel material combined is at least about 1 micrometer.

A4 1 19. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a carboxyl group and the hydrogel material is derived from
3 monomers selected from the group consisting of (meth)acrylic acid, 2-carboxyethyl
4 acrylate, N-acryloyl-aminohexanoic acid, N-carboxymethylacrylamide, 2-
5 acrylamidoglycolic acid, and derivatives thereof.

B1
1 20. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a sulfonate group and the hydrogel material is derived from
3 acrylamidomethyl-propane sulfonic acid monomers or derivatives thereof.

1 21. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a phosphate group and the hydrogel material is derived from N-
3 phosphoethyl acrylamide monomers or derivatives thereof.

1 22. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise an ammonium group and the hydrogel material is derived from
3 monomers selected from the group consisting of trimethylaminoethyl methacrylate,

William E. Rich, et al.
Application No.: 09/560,715
Page 3

PATENT

AG
Sub
B1

4 diethylaminoethyl methacrylate, diethylaminoethyl acrylamide, diethylaminoethyl
5 methacrylamide, diethylaminopropyl methacrylamide, aminopropyl acrylamide, 3-
6 (methacryloylamino)propyltrimethylammonium chloride, 2-aminoethyl methacrylate,
7 N-(3-aminopropyl)methacrylamide, 2-(t-butylamino)ethyl methacrylate, 2-(N, N-
8 dimethylamino)ethyl (meth)acrylate, N-(2-(N, N-dimethylamino))ethyl
9 (meth)acrylamide, N-(3-(N, N-dimethylamino))propyl methacrylamide, 2-
10 (meth)acryloyloxyethyltrimethylammonium chloride, 3-methacryloyloxy-2-
11 hydroxypropyltrimethylammonium chloride, (2-acryloyloxyethyl)(4-
12 benzoylbenzyl)dimethylammonium bromide, 2-vinylpyridine, 4-vinylpyridine,
13 vinylimidazole, and derivatives thereof.

1 23. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a hydrophilic group and the hydrogel material is derived from
3 monomers selected from the group consisting of N-
4 (meth)acryloyltris(hydroxymethyl)methylamine, hydroxyethyl acrylamide,
5 hydroxypropyl methacrylamide, N-acrylamido-1-deoxysorbitol,
6 hydroxyethyl(meth)acrylate, hydroxypropylacrylate, hydroxyphenylmethacrylate,
7 polyethylene glycol monomethacrylate, polyethylene glycol dimethacrylate, acrylamide,
8 glycerol mono(meth)acrylate, 2-hydroxypropyl acrylate, 4-hydroxybutyl methacrylate, 2-
9 methacryloxyethyl glucoside, poly(ethyleneglycol) monomethyl ether monomethacrylate,
10 vinyl 4-hydroxybutyl ether, and derivatives thereof.

1 24. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a hydrophobic group and the hydrogel material is derived from
3 monomers selected from the group consisting of N, N-dimethyl acrylamide, N, N-diethyl
4 (meth)acrylamide, N-methyl methacrylamide, N-ethyl methacrylamide, N-propyl
5 acrylamide, N-butyl acrylamide, N-octyl (meth)acrylamide, N-dodecyl methacrylamide,
6 N-octadecyl acrylamide, propyl (meth)acrylate, decyl (meth)acrylate, stearyl
7 (meth)acrylate, octyl-triphenylmethylacrylamide, butyl-triphenylmethylacrylamide,

William E. Rich, et al.
Application No.: 09/560,715
Page 4

PATENT

8 octadecyl-triphenylmethylacrylamide, phenyl-triphenylmethylacrylamide, benzyl-
9 triphenylmethylacrylamide, and derivatives thereof.

1 25. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a metal chelating group and the hydrogel material is derived
3 from monomers selected from the group consisting of N-(3-N, N-
4 biscarboxymethylamino)propyl methacrylamide, 5-methacrylamido-2-(N, N-
5 biscarboxymethylamino)pentanoic acid, N-(acrylamidoethyl)ethylenediamine N, N', N'-
6 triacetic acid, and derivatives thereof.

1 26. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a reactive group and the hydrogel material is derived from
3 monomers selected from the group consisting of glycidyl acrylate, acryloyl chloride,
4 glycidyl(meth)acrylate, (meth)acryloyl chloride, N-acryloxysuccinimide, vinyl azlactone,
5 acrylamidopropyl pyridyl disulfide, N-(acrylamidopropyl)maleimide, acrylamidodeoxy
6 sorbitol activated with bis-epoxirane compounds, allylchloroformate, (meth)acrylic
7 anhydride, acrolein, allylsuccinic anhydride, citraconic anhydride, allyl glycidyl ether,
8 and derivatives thereof.

1 27. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a thioether group and the hydrogel material is derived from
3 thiophilic monomers selected from the group consisting of 2-hydroxy-3-
4 mercaptopyridylpropyl (methacrylate), 2-(2-(3-
5 (meth)acryloxyethoxy)ethanesulfonyl)ethylsulfanyl ethanol, and derivatives thereof.

1 28. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a biotin group and the hydrogel material is derived from biotin
3 monomers selected from the group consisting of N-biotinyl-3-
4 (meth)acrylamidopropylamine and derivatives thereof.

B1
A4

William E. Rich, et al.
Application No.: 09/560,715
Page 5

PATENT

1 29. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a boronate group and the hydrogel material is derived from
3 boronate monomers selected from the group consisting of N-(m-dihydroxyboryl)phenyl
4 (meth)acrylamide and derivatives thereof.

1 30. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a dye group and the hydrogel material is derived from dye
3 monomers selected from the group consisting of N-(N'-dye coupled aminopropyl)
4 (meth)acrylamide and derivatives thereof.

1 31. (Once amended) The probe of claim 18 wherein the binding
2 functionalities comprise a cholesterol group and the hydrogel material is derived from
3 cholesterol monomers selected from the group consisting of N-cholesteryl-3-
4 (meth)acrylamidopropylamine and derivatives thereof.

1 32. (Once amended) A probe that is removably insertable into a mass
2 spectrometer, the probe comprising a substrate having a surface and a plurality of
3 particles that are substantially uniform in diameter on the surface, the particles
4 comprising binding functionalities for binding with an analyte detectable by the mass
5 spectrometer.

A5 1 76. (New) The probe of claim 1 wherein the binding functionality is
2 attached to said surface via a moiety that is derived from a reactive group selected from
3 an epoxide and a carbonyldiimidazole.

1 77. (New) The probe of claim 1 wherein the hydrogel material is
2 derived from monomers selected from the group consisting of 3-
3 (methacryloylamino)propyltrimethylammonium chloride, 2-acrylamidoglycolic acid
4 and 5-methacrylamido-2-(N, N-bis(carboxymethylamino)pentanoic acid.

William E. Rich, et al.
Applicati n No.: 09/560,715
Page 6

PATENT

- AS
- 1 78. (New) The probe of claim 1 wherein the hydrogel material
2 comprises cellulose or dextran.
- 1 79. (New) The probe of claim 1 wherein the surface is substantially
2 smooth.
- 1 80. (New) The probe of claim 1 wherein the hydrogel is about 1
2 micrometer thick.
- 1 81. (New) The probe of claim 1 wherein the substrate comprises an
2 insulating material.
- 1 82. (New) The probe of any of claims 1-4, 6-11, 13-31 or 76-81
2 wherein the surface of the substrate is conditioned with a coupling agent and the hydrogel
3 material adheres to the surface through a covalent interaction with the coupling agent.
- 1 83. (New) The probe of any of claims 1-4, 6-10, 14-31 or 76-81
2 wherein the hydrogel is attached to the surface in a plurality of discontinuous spots.
- 1 84. (New) The probe of claim 82 wherein the coupling agent is a
2 silane-based agent.
- 1 85. (New) The probe of claim 82 wherein the hydrogel is attached to
2 the surface in a plurality of discontinuous spots.
- 1 86. (New) The probe of claim 1 wherein the binding functionality is
2 attached to said surface via a moiety that is derived from a reactive group selected from
3 an epoxide and a carbonyldiimidazole.
- 1 87. (New) The probe of claim 32, 36 or 86 wherein the particles are
2 comprised of crosslinked polymers.

William E. Rich, et al.
Application No.: 09/560,715
Page 7

PATENT

AS 1 88. (New) The probe of claim 87 wherein the crosslinked polymers
2 comprise polystyrenes.

1 89. (New) The probe of claim 87 wherein the crosslinked polymers
2 comprise polysaccharides, agarose, dextran, methacrylates or functionalized silicon
3 dioxide.

1 90. (New) The probe of claim 87 wherein the particles comprise a
2 latex.

1 91. (New) The probe of claim 90 wherein the plurality of particles
2 have an average diameter of between about 0.1 μm to about 100 μm .

1 92. (New) The probe of claim 90 wherein the plurality of particles
2 have an average diameter of between about 1 μm to about 10 μm .

1 93. (New) The probe of claim 1 wherein the hydrogel material is less
2 than about one micrometer thick.

REMARKS

The Restriction Requirement

The Examiner has restricted the claims as filed into four Groups. Group I encompasses claims 1-36, drawn to a probe for a mass spectrometer. Group II encompasses claims 37-46, drawn to a system for detecting an analyte that includes the probe. Claims 47-59, drawn to a method of making the probe are within Group III. Group 4 includes claims 60-75, directed to a method of detecting an analyte.

→ In response to the Restriction Requirement, Applicants elect the claims of Group I for prosecution on the merits. Applicants respectfully traverse the Restriction Requirement. The embodiment of the invention currently defined by the claims as filed includes a probe, and methods of making and using the probe. Thus, each of the claims emerges out of a common inventive idea or concept. Applicants assert that the